UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/681,855	10/07/2003	Mark D. Bednarski	067425-5001-US	7135

67374 7590 06/23/2008

MORGAN, LEWIS & BOCKIUS, LLP
ONE MARKET SPEAR STREET TOWER
SAN FRANCISCO, CA 94105

EXAMINER	
ANDERSON, JAMES D	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
06/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/681,855	BEDNARSKI ET AL.	
	Examiner	Art Unit	
	JAMES D. ANDERSON	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 March 2008 and 12 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *3,11 and 20-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-10,12-19,32 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-33 are presented for examination

Applicants' amendment filed 3/20/2008 and Supplemental Response/Amendment filed 6/12/2008 have been received and entered into the application. Accordingly, claims 1-2, 4, 8-9, and 15-18 have been amended per the claim amendment filed 3/20/2008 and claims 32-33 have been added per the claim amendment filed 6/12/2008.

Pursuant to Applicants' election of Group I, claims 1-2 and 4-19, and the specie 1,3,3-trinitroazetidine in the reply filed 5/4/2007, claims 3, 11, and 20-31 remain withdrawn from consideration. Claims 1-2, 4-10, 12-19, and 32-33 are presently under examination and are the subject of this Office Action.

Applicants' arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Response to Arguments

Applicant's arguments filed 3/20/2008 and 6/12/2008 have been fully considered and are persuasive in part.

With regard to the 35 U.S.C. 101 rejection of claims 1, 2, 4-10, and 12-19 as lacking patentable utility, the Declaration of Richard Trecartin under 37 C.F.R. 1.132 is persuasive to the

extent that the cited 60/890,167 application demonstrates that the X-nitro compound ABDNAZ inhibits HL60 (leukemia) cell proliferation. Accordingly, the instant claims are deemed to have the utilities as set forth in the instant specification.

With regard to the 35 U.S.C. 112, 1st Paragraph rejection of claims 1, 2, 4-9, and 12-19 as failing to comply with the written description requirement, the Examiner is not persuaded that the claimed "X-nitro compound[s]" which comprise "a nitrocarbon", "a nitroamine", or "a nitrocarbon and a nitroamine" are adequately described in the specification. Applicants argue that the specification discloses that X-nitro compounds are "generally organic compounds substituted with one or more nitro groups" and further discloses physical properties of the claimed X-nitro compounds. As such, Applicants assert that the specification "fully lays out structures, formulae, names, and properties" of the X-nitro compounds recited in the claims. While it is certainly true that the specification sets forth the names of 11 specific examples of such compounds in the specification at page 6, lines 17-26 and structures and formulae at page 7, the fact remains that, other than these specific examples (which are not deemed to be representative of the claimed genus of "X-nitro compound"), the specification only provides a description of the claimed compounds in most general terms. In other words, Applicants describe the claimed X-nitro compounds as "organic compounds substituted with one or more nitro groups" (page 5, lines 7-8), which include compounds where the nitro group is bonded to a carbon atom or bonded to a nitrogen atom (page 5, lines 23-24). This description quite literally encompasses any organic compound having a nitro group. However, other than the 11 species exemplified in the disclosure, Applicants provide no specific description of the claimed X-nitro compounds that would allow one skilled in the art to immediately envisage the claimed

compounds. Accordingly, the rejection is maintained for the reasons of record and reiterated below.

With regard to the 35 U.S.C. 112, 1st paragraph rejection of claims 1, 2, 4-10, and 12-19 as failing to comply with the enablement requirement, Applicants argue that the specification of U.S. Provisional Application No. 60/890,167 (see Trecartin Declaration submitted 3/20/2008) shows positive in vitro and in vivo results for ABDNAZ in various cancer models. As such Applicants assert that they have shown that "X-nitro compounds can be used to treat conditions such as cancer" (see Response filed 3/20/2008 at page 10). In the Supplemental Response filed 6/12/2008, Applicants submit Declarations under 37 C.F.R. 1.132 by Dr. Bernacki ("Bernacki Declaration") and Dr. Knox ("Knox Declaration"). Applicants assert that the Bernacki Declaration establishes a nexus between the disclosure in the specification and the results presented in the declaration and that the Knox Declaration addresses the activity of ABDNAZ in a hypoxic environment. Based upon these two declarations, Applicants submit that the specification enables the pending claims. The Examiner has carefully considered the declarations of Drs. Bernacki and Knox but is not persuaded that the data presented therein correlates to a high probability of "treating or preventing cancer", "treating hypoxic tumor cells", or "treating or preventing solid tumors" comprising administering "to a patient" an "X-nitro compound". Exhibit 2 in the Bernacki Declaration relates to the cytotoxicity of high energy compounds against HT29 (colon cancer) cells *in vitro*. The IC_{50} values of said compounds are presented in "mM" (millimolar). For reference, it is noted that cisplatin was determined to have an IC_{50} of 0.004 mM (4 μM) in this assay. The IC_{50} values of the tested high energy compounds ranged from 0.001 mM (1 μM) (ABDNAZ) to 5.45 mM (5,450 μM) (PETN), a 5,450-fold

difference in activity in this assay. Clearly, such a broad spectrum of cytotoxic activity does not provide any reasonable expectation that a given X-nitro compound will have cytotoxic activity against HT29 cells, let alone cancer cells generally. Further, one skilled in the art would recognize that a compound having an IC_{50} of close to 1 mM *in vitro* would be considered to be "inactive" and highly unlikely to have therapeutic activity *in vivo*. In other words, almost any small organic molecule administered at a high enough dose would be cytotoxic to cancer cells *in vitro*. Only 14 out of 27 tested high energy compounds had IC_{50}s of less than 100 μM, and 9 of these 14 compounds were structurally related nitroazetidine compounds (Exhibit 3). While ABDNAZ was shown to have *in vitro* cytotoxic activity against multiple cancer cell lines, there is no evidence that such broad spectrum *in vitro* activity extends to other X-nitro compounds (Exhibit 5). Further, while ABDNAZ was shown to have *in vivo* activity against SCC VII tumors implanted in mice, there is no evidence that any other X-nitro compounds have any *in vivo* therapeutic efficacy (Exhibit 6, pages 9-10). Accordingly, while Applicants have presented evidence that ABDNAZ would be reasonably expected to have *in vivo* therapeutic activity against cancer and solid tumors as instantly claimed, the Examiner is not persuaded that Applicants have enabled one skilled in the art to practice the claimed methods of "treating or preventing cancer", "treating hypoxic tumor cells", or "treating or preventing solid tumors" comprising administering "to a patient" an "X-nitro compound" as broadly recited in the claims. The rejection of claims 1-2, 4-10, and 12-19 (now 1-2, 4-10, 12-19, and 32-33) is maintained for the reasons of record and reiterated below.

Claim Rejections - 35 USC § 112 (1st Paragraph)

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-9, 12-19, and 32-33 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a Written Description requirement.

In the present case, the claims and specification refer to methods of using an "X-nitro compound" to treat or prevent cancer. Pages 5-6 of the specification discuss what compounds are considered to be "X-nitro compounds". In this regard, the specification teaches that X-nitro compounds are generally "organic compounds substituted with one or more nitro groups" (page 5, lines 7-8). Such compounds include compounds where the nitro group is "bonded to a carbon atom to form a nitrocarbon, to a nitrogen to form a nitroamine, to a sulfur atom or to a phosphorous atom and any combination thereof" (*id.* at lines 23-25). Examples of specific X-nitro compounds are disclosed at page 6, lines 17-26, some of whose structures are shown on page 7. It appears that 11 species of X-nitro compounds are specifically disclosed. The term "X-nitro compound" appears to be a designation only used by Applicants. For example, no other patents of patent application publications use the term "X-nitro compound". As such, one skilled in the art has no way of identifying an "X-nitro compound" other than by reading Applicants' disclosure.

Regarding the requirement for adequate written description of chemical entities, Applicant's attention is directed to the MPEP §2163. In particular, *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089, 118 S. Ct. 1548 (1998), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plain for obtaining the claimed chemical invention." *Eli Lilly*, 119 F.3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications under the 35 U.S.C. 112.I "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia*, "functional characteristics when coupled with a known or disclosed correlation between function and structure..." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 316, 1324-25 (Fed. Cir. 2002) (quoting *Guidelines*, 66 Fed. Reg. at 1106 (emphasis added)). Moreover, although *Eli Lilly* and *Enzo* were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in general. *Univ. of Rochester v. G.D. Searle & Co.*, 249 Supp. 2d 216, 225 (W.D.N.Y. 2003).

Applicants have failed to provide any reasonably specific structural characteristics, chemical formula, name(s) or physical properties, aside from the express identification of the 11 compounds on page 7 of the specification, that would provide adequate written description of the genus of compounds encompassed by “X-nitro compound”. A reasonable interpretation of the scope of such compounds is that they encompass any compound having a nitro group. Such a

limitation is akin to claiming methods of treating cancer by "administering a compound having an alcohol group", where only 11 such compounds are explicitly disclosed. Clearly, one skilled in the art is not presented with an adequate written description of exactly what compounds are intended for use in the claimed methods. With regard to new claims 32-33, Applicants have provided no description with respect to what X-nitro compounds, out of all X-nitro compounds that exist in the art, would be expected to have the claimed enthalpy of formation.

Accordingly, while Applicants have described 11 species of the claimed genus of compounds, they have not described X-nitro compounds with any reasonable specificity so as to clearly convey that they were in possession of the full scope of the claimed subject matter at the time the invention was made.

Claims 1-2, 4-10, 12-19, and 32-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating cancer or solid tumors comprising administering ABDNAZ, does not reasonably provide enablement for "treating or preventing cancer", "treating hypoxic tumor cells", or "treating or preventing solid tumors" comprising administering "to a patient" an "X-nitro compound" as broadly recited in the instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This is a Scope of Enablement rejection.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.

In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence or absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA

[1] As pointed out by the court in *In re Angstadt*, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the *Wands* factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill of those in the art

The invention relates to the treatment or prevention of cancer (claim 1), treatment of tumors (claims 15 and 16), and treatment or prevention solid tumors (claims 17-18) by administering an "X-nitro compound" alone, or in combination with radiation or other anticancer agents.

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. The artisan using Applicant's invention would generally be a physician with a M.D. degree and several years of experience.

That factor is outweighed, however, by the unpredictable nature of the art. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), *Nationwide Chemical Corporation, et al. v. Wright, et al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances), *Ex parte Sudilovsky* 21 USPQ2d 1702 (Appellant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) *In re Wright* 27 USPQ2d 1510 (the

physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain). As illustrative of the state of the art, the examiner cites Sausville *et al.* (Cancer Research, 2006, vol. 66, pages 3351-3354) and Johnson *et al.* (British J. of Cancer, 2001, 84(10):1424-1431).

Sausville *et al.*, cited for evidentiary purposes, teaches that traditionally explored tumor model systems are insufficient to predict how actual human beings will respond to treatment in the clinic (page 3351, left column). Even when drugs with evidence of anticancer activity in preclinical *in vivo* models are given their maximum tolerated dose in humans, they frequently fail to produce useful activity in humans (*id.*). Also, with regard to unpredictability, Johnson *et al.*, also cited for evidentiary purposes, teach that the *in vivo* activity of 39 different agents in a particular histology in a tumor model did not correlate to activity in the same human cancer. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Further, the mode of action of anticancer agents is often unknown or very unpredictable and administration of such agents is often accompanied by undesirable side effects.

The Examiner also refers to the Declaration of Dr. Bernacki, wherein the cytotoxicity of high energy compounds against HT29 (colon cancer) cells *in vitro* is shown. The IC_{50} values of said compounds are presented in "mM" (millimolar). For reference, it is noted that cisplatin was found to have an IC_{50} of 0.004 mM (4 μM) in this assay. The IC_{50} values of the tested compounds ranged from 0.001 mM (1 μM) (ABDNAZ) to 5.45 mM (5,450 μM) (PETN), a 5,450-fold difference in activity in this assay. Clearly, such a broad spectrum of cytotoxic activity does not provide any reasonable expectation that a given X-nitro compound will have

cytotoxic activity against HT29 cells *in vitro*, let alone cancer cells generally, let alone *in vivo* therapeutic efficacy as claimed.

These articles plainly demonstrate that the art of treating cancer, particularly in humans, is extremely unpredictable, particularly in the case of a single compound or genus of compounds being used to treat any and all cancers.

2. The breadth of the claims

The claims are extremely broad insofar as they disclose the general treatment and prevention of cancer and tumors by administering an "X-nitro compound".

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for determining the particular administration regimens (*e.g.*, dosages, timing, administration routes, etc.) necessary to treat (let alone prevent) all of the various cancers and tumors claimed, particularly in humans. The direction concerning treating cancer is found in the specification at pages 20-25, which merely states Applicants' intention to do so by providing cellular assays and *in vivo* assays for determining the cell growth inhibitory effect of the claimed compounds. No compounds appear to have actually been tested in these assays. Applicants describe formulations at pages 10-17. Doses required to practice their invention are described at page 13. A 100,000-fold range of doses is recommended (*e.g.*, 0.001 to 100 mg/kg). Since no X-nitro compound as specifically disclosed in the specification has ever been used to treat any human cancer, how is the skilled physician to know what dose to use for each of these pathologically different cancers and

structurally diverse compounds? There are no guidelines for determining the doses needed to treat a carcinoma *vs.* a myeloid disorder *vs.* adenoma *vs.* a leukemia. Are the identical doses to be used for treating these unrelated cancers? There is both an *in vitro* cellular assay and an *in vivo* assay described in pages 20-25 (with no data) and it is unclear if these assays correlate to all of the cancers encompassed by the claims. As discussed *supra*, *in vitro* assays are generally not predictive of activity in human subjects. There is no working example of treatment (let alone prevention) of any cancer or tumor in cells, animals or man. It is noted, however, that the Declaration of Dr. Bernacki submitted 6/12/2008 presents evidence that *some* X-nitro compounds are cytotoxic to HT29 cells *in vitro* and that one X-nitro compound (ABDNAZ) inhibits SCC tumor growth *in vivo*.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art (as discussed *supra*) and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that the instantly claimed X-nitro compounds (which the Examiner notes includes explosives such as nitroglycerin and TNT) could be predictably used as a treatment, let alone prevention, for all cancerous cell growth as inferred in the claims and contemplated by the specification.

Genentech Inc. vs. Nova Nordisk states, "[A] patent is not a hunting license. It is not a reward for a search but a compensation for its successful conclusion and 'patent protection' is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" (42 USPQ 2d 1001, Fed. Circuit 1997).

In the instant case, Applicants have presented a general idea that any and all X-nitro compounds (*i.e.*, any organic compound having one or more nitro groups) can be somehow activated *in vivo* so as to be useful in the treatment of cancerous cell growth. However, the claims encompass a multitude of compounds (literally hundreds of millions of structurally distinct compounds) having a plethora of chemically and biologically distinct substituents. Applicants specifically disclose eleven X-nitro compounds having no similarity other than the presence of one or more nitro groups. None of these compounds have been shown to inhibit any cancerous cell growth in vivo. One skilled in the art would not reasonably expect that any compound having a nitro group would have biological activity, let alone activity in preventing or treating any and all cancers as claimed. The only common structural feature of the disclosed X-nitro compounds is the $-NO_2$ moiety. Given the extremely diverse compounds encompassed by the claims and the absence of working examples in the specification, the skilled artisan cannot predict what structural features would be important for anticancer or antitumor activity. Clearly, the presence of a nitro group is not sufficient to provide an organic compound with anticancer activity. For example, as Applicants disclose on page 5, lines 15-17 of the specification, X-nitro compounds include "those nitro compounds that decompose with explosive force upon activation (*e.g.*, nitroglycerin, trinitrotoluene trinitrobenzene, etc.)". It appears that Applicants are suggesting that administration of TNT (and other explosives) to a patient will effectively treat cancer.

Determining if any particular claimed compound would treat any particular cancerous disease state would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it to clinical trials or to testing in an assay known to correlate to clinical efficacy

of such treatment. This is undue experimentation given the limited guidance and direction provided by Applicants. As noted *supra*, even *in vitro* and *in vivo* assays do not always correlate to efficacy in humans and are not generally predictive of clinical efficacy.

Accordingly, the instant claims do not comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Application No. 11/502,810

Claims 1, 4, 7-8, and 15-18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 17-21 of copending Application No. 11/502,810. Although the conflicting claims are not identical, they are not

patentably distinct from each other because the designation "X-nitro compound" in the instant claims reasonably encompasses the compounds of Formula I as recited in claim 1 of the '810 application. Claims 17-21 of the '810 application recite methods of treating the same cancers and tumors as the instant claims by administering a compound of claim 1. Accordingly, the instantly claimed methods are not patentably distinct from the methods claimed in the '810 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. USP No. 5,521,203 discloses compounds for treating a patient having a solid tumor in which it is known or suspected that hypoxic cells are present. The compounds disclosed in '203 are "X-nitro compounds" as recited in the instant claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614